REMARKS

Claims 8, 11, 14-22 and 24-37 are in the application. Solely to compact prosecution and without prejudice or disclaimer Applicants herewith cancel claims 1-7, 9, 10, 12 and 13. Applicants expressly reserve the right to pursue all cancelled subject matter. Applicants herewith add claims 38-72, support for which is found, *inter alia*, in the claims as filed, throughout the specification including the Sequence Listing and Figures 24-27. No new matter is added. Entry and consideration of the Amendment is respectfully requested.

I. Priority Should Be Accorded For Claims 8, 11, 14-22 and 24-72 Under 35 U.S.C. § 120

At page 3 of the Office Action, the Office acknowledges that the Applicants *disagree* that claims 1-3, 6-19, 22, 24-27, 30-34 and 37 do not benefit under 35 U.S.C. § 120 to the earlier filing dates of Applicants' priority documents. The Office predicates the denial on the rejection of claims 1-3, 6-19, 22, 24-27, 30-34 and 37 under 35 U.S.C. § 112, first paragraph (i.e., alleged lack of a written description and enablement) and an alleged improper incorporation by reference although the Office simultaneously admits that Applicants' priority document "describes a composition comprising an antibody and a second agent" at page 3 of the Office Action. The rejections of claims 1-3, 6-19, 22, 24-27, 30-34 and 37 under 35 U.S.C. § 112, first paragraph (i.e., lack of a written description and enablement) and alleged improper incorporation by reference are addressed in detail below, *inter alia*, at Sections II-VIII. After consideration of the causal issues addressed below and withdrawal of the objections and rejections, Applicants kindly request that the Office acknowledge Applicant's priority for claims 8, 11, 14-22 and 24-72.

II. The Declaration Is Proper Under 37 C.F.R. § 1.132 and Claims 8-19, 22, 24, 26, 27, 30, 31 and 37 Are Novel Under 35 U.S.C. 102(a)

At page 4 of the Office Action, the Office acknowledges that the Declaration under 37 C.F.R. § 1.132 is sufficient to overcome the rejection of claims 1-3, 5-19, 22, 24, 26, 27, 30, 31 and 37 under 35 U.S.C. 102(a) as being anticipated by Maloney *et al.* (*Cancer Research*, 63:5073-5083 (2003)).

III. The Specification Is Proper Under 35 U.S.C. §132(a)

At page 4 of the Office Action, the Office maintains the objection under 35 U.S.C. §132(a) to the Amendment filed April 16, 2007 because the Amendment allegedly introduces new matter into the disclosure. The Office alleges that the Applicants did not point with *any* particularity to the relevant disclosure in DeVita *et al.* in the specification and because Applicants improperly amended the specification to include sections of DeVita *et al.*

The Offices' position ignores binding authority. As the record indicates, Rule 37 C.F.R. § 1.57 states that incorporation by reference is accomplished by expressing a clear intent to incorporate by reference (*i.e.,* by using the words "incorporate" and "reference") and by clearly identifying the referenced information (*i.e.,* a patent, application or publication). The M.P.E.P. clearly states, "an application may attempt to incorporate the content of another document or *part thereof* by reference to the document in the text of the specification. The information incorporated is as much a part of the application as filed as if the text was repeated in the application, and should be treated as part of the text of the application as filed." Emphasis added. M.P.E.P. § 2163.07(b).

At page 5 and 15 of the Office Action, the Office admits that the Applicants expressed a clear intent to incorporate by reference the content of the publications cited in the specification.

At paragraph 93 of the specification, Applicants explicitly identify the incorporated publication DeVita *et al.* Thus, the April 16, 2007 Amendment to the specification incorporating DeVita *et al.* is in compliance with 37 C.F.R. § 1.57. The Office attempts to factually distinguish the law, for example the holding in *Ex parte Maziere* (Appeal No. 92-3407), from the present facts by arguing that *Ex parte Maziere* dealt with incorporation by reference of information in a U.S. patent application not non-patent literature however, this distinction appears illogical and without legal basis as the Court in *Ex parte Maziere* did not categorically narrow the holding as the Office suggests. The Office fails to substantively address the holding in *Ex parte Maziere*.

The Examiner cites to *dicta* in *Advanced Display Systems Inc. v. Kent State University* (54 USPQ2d 1673) as controlling however, the Examiner failed to appreciate that, on the issue of incorporation by reference (and therefore the ultimate issue of anticipation), the Court in *Advanced Display Systems* remanded the case for a new trial solely on the procedural ground of an improper magistrate instruction to the jury. The Office's attempt to circumvent *Ex parte Mazier* ignores the directly relevant holding of Judges Lovell, Goolkasian, and W. Smith of the Board. Applicants remind the Office that the holding in *Ex parte Mazier* is binding, wherein the Judges indicated "the Applicants...were quite correct in not further burdening the record of that file by including the text which was incorporated by reference." Page 3, *Ex parte Maziere.*

The Office also ignores the holding in *Southern Clay Products, Inc., v. United Catalysts, Inc.*, 43 Fed.Appx. 379, 64 U.S.P.Q.2d 1606 (No. 01-1382) (July 26, 2002, rehearing and Rehearing En Banc Denied Sept. 4, 2002), wherein the Court disagreed with party Southern Clay's argument that "...merely citing to a reference is not sufficient for incorporation of it, and that Clocker does not clearly identify which material in Cohn is meant to be incorporated...,"

holding instead that "we disagree. Clocker specifically identifies that Cohn is relevant for its bond-breaking methods…By citing to and specifically identifying the bond-breaking techniques discussed by Cohn, Clocker has demonstrated the intent to make that information part of the specification." The Applicants have gone far beyond reference to a generic technique but rather particularly teach, i.e., in the specification at paragraph 94:

> "[0094] The therapeutic agents that can be combined with EM164 for improved anti-cancer efficacy include diverse agents used in oncology practice (Reference: Cancer, Principles & Practice of Oncology, DeVita, V. T., Hellman, S., Rosenberg, S. A., 6th edition, Lippincott-Raven, Philadelphia, 2001), such as docetaxel, paclitaxel, doxorubicin, epirubicin, cyclophosphamide, trastuzumab (Herceptin), capecitabine, tamoxifen, toremifene, letrozole, anastrozole, fulvestrant, exemestane, goserelin, oxaliplatin, carboplatin, cisplatin, dexamethasone, antide, bevacizumab (Avastin), 5-fluorouracil, leucovorin, levamisole, irinotecan, etoposide, topotecan, gemcitabine, vinorelbine, estramustine, mitoxantrone, abarelix, zoledronate, streptozocin, rituximab (Rituxan), idarubicin, busulfan, chlorambucil, fludarabine, imatinib, cytarabine, ibritumomab (Zevalin), tositumomab (Bexxar), interferon alpha-2b, melphalam, bortezomib (Velcade), altretamine, asparaginase, gefitinib (Iressa), erlonitib (Tarceva), anti-EGF receptor antibody (Cetuximab, Abx-EGF), epothilones, and conjugates of cytotoxic drugs and antibodies against cell-surface receptors. Preferred therapeutic agents are platinum agents (such as carboplatin, oxaliplatin,

cisplatin), taxanes (such as paclitaxel, docetaxel), gemcitabine, and camptothecin."

The Office also failed to appreciate Applicants' particular teachings at paragraph 148 of the specification:

> "[0148] For these combination therapies, EM164 is combined with one or more anti-cancer agents of diverse mechanisms of action such as alkylating agents, platinum agents, hormonal therapies, antimetabolites, topoisomerase inhibitors, antimicrotubule agents, differentiation agents, antiangiogenic or antivascularization therapies, radiation therapy, agonists and antagonists of leuteinizing hormone releasing hormone (LHRH) or gonadotropin-releasing hormone (GnRH), inhibitory antibodies or small molecule inhibitors against cell-surface receptors, and other chemotherapeutic agents (Reference: Cancer, Principles & Practice of Oncology, DeVita, V. T., Hellman, S., Rosenberg, S. A., 6th edition, Lippincott-Raven, Philadelphia, 2001). In one example, the combination of an LHRH antagonist antide (0.1 to 10 micromolar) and EM164 antibody (0.1 to 10 nanomolar) inhibited the proliferation of MCF-7 breast cancer cells significantly more than that with either EM164 or antide alone. In an example of a combination therapy with a platinum agent, the combined treatment with EM164 antibody (10 microgram/ml) and cisplatin (0.1-60 microgram/ml) resulted in a greater inhibition of the proliferation and survival of MCF-7 breast cancer cells in comparison to the inhibition by either EM164 antibody or cisplatin alone."

The Office's objection ignores *In the Matter of the APPLICATION of Raymond O. VOSS* (Patent Appeal No. 76-710) wherein the Board held, it "was clear that appellant intended the 'discussion of glass-ceramic materials and their production' in Stookey '971 to become part of his parent application. See *In re Lund*, 376 F.2d 982, 989 (1967). The board erred in finding otherwise. Compare the incorporating language quoted, supra, in the parent application with the language in *In re Hughes*, 550 F.2d 1273 (Cust. & Pat.App.1977), where a statement, 'Reference is made to application Ser. No. 131,108 for complete descriptions of methods of preparing aqueous polymeric dispersions applicable in the hereinafter described invention,' was held to incorporate the disclosure of such methods into the patent in question." The Court concluded, "appellant's parent application complies with the requirements of 35 U.S.C. 112, first paragraph and that appellant is entitled to his filing date under 35 U.S.C. 120."

Consistent with 35 U.S.C. § 132(a), Rule 37 C.F.R. § 1.57, 35 U.S.C. § 112, first paragraph, M.P.E.P. § 2163.07 and the holdings in *Ex parte Maziere*, *Southern Clay Product* and *In the Matter of the APPLICATION of Raymond O. VOSS,* Applicants' incorporation by reference is proper. Withdrawal of the new matter objection is therefore kindly requested.

IV. The Request for Rejoinder of Claims 22, 30, 31, and 32 is Maintained

Applicants maintain their request for rejoinder, as a matter of right, of the claims of Group III, upon allowance of the elected claims. M.P.E.P § 821.04.

V. Claim 8, 11, 14-22, 24, 26, 27, 30-34, and 37 are Adequately Described Under 35 U.S.C. § 112, First Paragraph

At page 6 of the Office Action, the Office maintains the rejection of claims 1-3, 6-19, 22, 24, 26, 27, 30-34 and 37 under 35 U.S.C. § 112, first paragraph, for allegedly lacking a written

description because a subgenera of a genus of antibodies which specifically bind IGF-IR allegedly lack written support in the specification.

The rejection is moot as to claims 1-3, 6, 7, 9, 10, 12 and 13. Solely to advance prosecution, Applicants herewith amend the claims without prejudice or disclaimer. Applicants' Amendment overcomes the rejection.

For the record, the Examiner asserts that the claims lack a written description for antibodies that bind to IGF-IR (i.e., the same specificity as EM164) with fewer than six CDRs or contain any variation among their sequences. In making the arguments the Examiner improperly relies on several antiquated references that were published more than a decade prior to Applicants' filing date and demonstrate the opposite of that which he concludes. First, the Examiner relies on *Mariuzza et al.* stating, "it is apparent that one of skill in the art could not immediately envision, recognize or identify antibodies that speficially bind to IGF-IR having the same binging specificity as murine antibody EM164 unless the antibody comprised a light chain variable domain and a heavy chain variable domain having the CDRs of murine EM164 in their proper contect of 'framework' regions." Office Action, pages 9-10. However, *Mariuzza et al.*, as cited by the Office, does not disclose such a statement but does indicate, "heteroclitic antibodies that might have higher affinities for heterologous, closely related antigens" exist, that "somatic mutations in the antibody gene could give a better fit between antigen and antibody" and that "since the substitution of His for Gln in the interface is not steriochemically forbidden and may even be favored, the explanation for the dramatic decrease in affinity for D1.3 for lysozymes with His at position 121 lies elsewhere." *Mariuzza et al.*, pages 146 and 149, respectively. The Examiner cites to *Vajdos et al.* as proof of "a near consensus in the art that the specificity of an antibody is mostly dependent upon the identities of the CDRs" however, *Vajdos*

et al. clearly states, "most of the wt/mut ratios for the display section were close to 1.0, indicating that the mutations did not significantly affect Fab2C4 display levels (Tables 3 and 4)." *Vajdos et al.,* page 419.

The references are cited at page 17-24 of the Office Action for similar reasons (i.e., to buttress arguments regarding an alleged lack of enablement due to unpredictability in the art). In addition, the Examiner cites Rudikoff *et al.* (Office Action, page 19) and Watkins *et al.* (Office Action, page 22) to prove that it is highly unpredictable which antigen an antibody will bind based on homology alone however, the Rudikoff *et al.* states the opposite. Rudikoff *et al.* disclose that SI07 subclones are vastly antigen reactive, since only "0.1-1%" of the clones do not precipitate in soft agar assays. Page 1980, Results and Discussion, first sentence. Furthermore, at page 1982, the researchers conclude, "[w]e have characterized another primary variant of S107 that has decreased antigen binding and a single amino acid substitution in the fifth residue of its J segment (39). However, it is clear that all substitutions need not and probably do not affect antigen binding. For example, the heavy chain from the P-Cho-binding myeloma protein M167 (35) differs from that of S107 at 13 positions (8 in hypervariable regions including a size difference) and yet has an association constant for hapten only slightly lower than S107. We have previously shown that, among anti-1,6-galactan-binding myeloma proteins, as many as eight or nine substitutions may occur in hypervariable regions with no significant effect on hapten affinity or specificity." Emphasis added. Thus, the reference as cited by the Examiner is an anomaly, and not representative of the state of the art, nor the Examiner's position. Regarding Watkins et al., even if the antibodies of Watkins *et al.* bind collagen, at no point do Watkins *et al.* suggest or demonstrate that the antibodies do not bind IGF-IR. Cross-reactive antibodies are known in the art. Functional variants and antibodies with fewer than six CDRs are

known in the art.[1] For example, on page 527, Aires da Silva *et al.* disclose the production of rabbit anti-Vif VH single-domain antibodies. Further, Tanaka *et al.* disclose the use of intracellular antibody capture using scFc phage antibody libraries, to isolate single-domain VH "intrabodies," which have been demonstrated to possess greater affinity for antigen than the parental antibody containing heavy and light chains. Page 1110, column 2, lines 44-48. Further, Tanaka *et al.* conclude that "binding of the anti-RAS scFv33 to antigen can occur through the VH domain alone." Page 1110, column 2, last sentence. Further still, on page 1115, column 2, first full paragraph, Tanaka *et al.* disclose that isolated VH domains are "ideal for binding specifically and with high affinity to antigen *in vivo*" and that "VL alone should possess the same property." Peterson *et al.* disclose that "a CDR is the smallest functional unit of an antibody" and states, "[T]he smallest functional unit of an antibody to be produced has been the CDR peptides . . . which can vary from eight to 20 amino acids" (page 314-315 and Figure 1C). Peterson further states that "[t]he affinity of a CDR is tested by its ability to compete with the parental antibody at its binding site. Berezov and colleagues (2001) demonstrated that a peptide designed from the sequence of the third CDR of an anti-Her2/neu antibody heavy chain sequence was able to bind to the receptor and disable its tyrosine kinase activity. Another biologically active peptide derived from an antineurokinin receptor antibody by Wijkhuisen and coworkers (2003) was capable of antagonizing substance P-induced cAMP production." Peterson at page 315. See, Advances in Monoclonal Antibody Technology: Genetic Engineering of Mice, Cells and Immunoglobulins, Peterson NC, ILAR J. 46(3):314-319 (2005). Park et al., discloses

[1] A patent disclosure need not enable information within the knowledge of an ordinarily skilled artisan. *Chiron Corp. v. Genentech, Inc.*, 363 F.3d 1247, (Fed. Cir. 2004), petition for cer. Filed, Oct. 4, 2004. Extensive screening to isolate a claimed cell was not undue when the required methods are routine in biotechnology. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988).

AHNP which "is comparable in potency to the full-length monoclonal antibody and exhibits biochemical and biological properties that are predictive of therapeutic use." Page 194, second column, sentences 1-7. The reference further states, "the general approach described here may be considered a paradigm for development of specific receptor-based therapies..." The *general approach* is referenced to date back to as early as 1996 (see reference 19, Zhang et al.). Please note that AHNP was extensively analyzed and found to inhibit cell proliferation and anchorage independent growth (Figure 2); enhance apoptosis (Figure 4); and inhibit in vivo tumor growth (Figure 5). U.S. Patent No. 6,926,893, states, "another form of an antibody fragment is a peptide coding for a single [CDR] can be obtained by constructing genes encoding the CDR of an antibody of interest." Col. 9, lines 43-47.

The art references establish that prior to Applicants' filing date the state of the art of antibody production was such that a person of ordinary skill in the art would conclude, without question, that an antibody could be routinely made and used from a single CDR and that variations of an antibody wherein functional antibodies are obtained is routine in the art.

Withdrawal of the lack of written description rejection is respectfully requested.

VI. Claims 17, 30 and 32-34 Do Not Introduce New Matter Under 35 U.S.C. § 112, First Paragraph

At page 14 of the Office Action, the Office maintains the rejection of claims 2, 17, 30, and 32-34 under 35 U.S.C. § 112, first paragraph, for allegedly introducing new matter into the specification (*i.e.*, specifically, thalidomide, carmustine, pamidronate, prednisone, erythropoietin and bisphosphonate) because the specification allegedly fails to particularly point to the disclosure of these compounds in the reference that was incorporated by reference into the specification.

Applicants disagree. The rejection is moot as to claim 2. Solely to advance prosecution, Applicants herewith amend the claims without prejudice or disclaimer. Applicants' Amendment overcomes the rejection.

Applicants herewith incorporate and apply the argument set forth above, in section III, wherein Applicants assert that the Offices' position ignores binding authority. Rule 37 C.F.R. § 1.57 states that incorporation by reference is accomplished by expressing a clear intent to incorporate by reference (i.e., by using the words "incorporate" and "reference") and by clearly identifying the referenced information (i.e., a patent, application or publication). M.P.E.P. § 2163.07(b) states, "an application may attempt to incorporate the content of another document or *part thereof* by reference to the document in the text of the specification. The information incorporated is as much a part of the application as filed as if the text was repeated in the application, and should be treated as part of the text of the application as filed." Emphasis added. M.P.E.P. § 2163.07(b). The Applicants expressed a clear intent to incorporate by reference the content of the publications cited in the specification. Again, *Ex parte Maziere* (Appeal No. 92-3407) is binding on the Office however, the Office attempts to circumvent *Ex parte Mazier* and ignores the directly relevant holding of Judges Lovell, Goolkasian, and W. Smith of the Board, even though the Judges indicated "the Applicants…were quite correct in not further burdening the record of that file by including the text which was incorporated by reference." Page 3, *Ex parte Maziere.* The holding in *Southern Clay Products, Inc., v. United Catalysts, Inc.*, 43 Fed.Appx. 379, 64 U.S.P.Q.2d 1606 (No. 01-1382) (July 26, 2002, rehearing and Rehearing En Banc Denied Sept. 4, 2002), is consistent with Applicants position and express intent to make the incorporated disclosure in DeVita *et al.* part of the specification. The Applicants have gone far beyond reference to a generic technique but rather particularly teach

the diverse agents used in oncology practice herein incorporated for combination with EM164 for improved anti-cancer efficacy. *Inter alia*, Paragraphs 94 and 148, Specification.

The Office ignores *In the Matter of the APPLICATION of Raymond O. VOSS* (Patent Appeal No. 76-710) wherein the Board held, it "was clear that appellant intended the 'discussion of glass-ceramic materials and their production' in Stookey '971 to become part of his parent application and "appellant's parent application complies with the requirements of 35 U.S.C. 112, first paragraph and that appellant is entitled to his filing date under 35 U.S.C. 120." As in *In the Matter of the APPLICATION of Raymond O. VOSS*, the Applicants express a clear intent to incorporate and call out the diverse agents used in oncology practice herein incorporated for combination with EM164 for improved anti-cancer efficacy to be incorporated in the specification.

Consistent with 35 U.S.C. § 132(a), Rule 37 C.F.R. § 1.57, 35 U.S.C. § 112, first paragraph, M.P.E.P. § 2163.07 and the holdings in *Ex parte Maziere*, *Southern Clay Product, In the Matter of the APPLICATION of Raymond O. VOSS,* Applicants' incorporation by reference is proper. Withdrawal of the new matter objection is therefore kindly requested.

VII. Claims 8, 11, 14-22, 24, 26, 27, 30-34, and 37 are Enabled Under 35 U.S.C. § 112, First Paragraph

On page 17 of the Office Action, the Office maintains rejection to claims 1-3, 6-19, 22, 24, 26, 27, 30-34 and 37 under 35 U.S.C. § 112, first paragraph, for lacking enablement because the specification, does not allegedly reasonably provide enablement for making and using a composition comprising antibodies with the same binding specificity as murine antibody EM164 that are substantially devoid of agonist activity and that do not comprise the amino acid sequence of the 6 CDRs of antibody EM164.

The rejection is moot as to claims 1-3, 6, 7, 9, 10, 12 and 13. Solely to advance prosecution, Applicants herewith amend the claims without prejudice or disclaimer. Applicants' Amendment overcomes the rejection. Withdrawal of the lack of enablement rejection is therefore kindly requested.

For the record, the Examiner's position is contradictory to the Board's precedential decision, *Ex parte Kubin* (Appeal No. 2007-0819), wherein the Examiner rejected claims containing "at least 80% identity to" language in the absence of working examples by relying upon scientific literature that allegedly suggested that very small changes in a sequence, even one amino acid, result in a different function. In *Ex parte Kubin* claims directed to "polypeptides at least 80% identical to amino acids 22-221 of SEQ ID NO:2" were found enabled by the Board. The Board withdrew the Examiner's rejection because the amount of experimentation required to practice the claimed invention might have been extensive but would have been routine. The Board acknowledged that the specification did not disclose any variant of SEQ ID NO:2 within amino acids 22-221 however, the Board acknowledged the high skill level in the field, that the methods for making and screening the variant sequences were known in the art, and concluded that "the experimentation involved to produce other sequences within the scope of the claims would have been well within the skill of those in the art," and thus routine.

The Office's position is inconsistent with the Board's decision in *Ex parte* ABAD, wherein the Board addressed, "[w]ould it have required undue experimentation to make and/or use the full scope of a nucleic acid that has at least 90% sequence identity to SEQ ID NO: 1?" The Board concluded that "[i]t would not have required undue experimentation to practice of the full scope of the claimed invention. We note that if claims with 90% sequence identity are enabled, *a fortiori*, the dependent claims with narrower 95% sequence identity are also enabled."

Other than the fact that molecular biology is an unpredictable art, the remaining *Wands* factors favor Appellants, particularly "the amount of direction or guidance presented", "the state of the prior art" and "the relative skill of those in the art," *In re Wands*, 858 F.2d 731, 736 (Fed. Cir. 1988). See *Ex parte* ABAD; BPAI, Appeal 2007-4356. It is well settled that patent applicants are not required to disclose every species encompassed by their claims, even in an unpredictable art. *In re Angstadt*, 537 F.2d 498, 502-03, 190 USPQ 214, 218 (CCPA 1976).

The Office's assertions regarding the existence of a chance of a change in the specificity of Applicants' antibody as recited by the claims due to substitutions of individual CDR amino acids or combinations of CDR mutations that bind the same antigen, the deletion or insertion of amino acids in the variable regions or the CDRs as recited by the claims (i.e., 90% identity) renders Applicants' invention as recited by the claims unpatentable ignores the law. Assuming *arguendo* that a single claimed embodiment is inoperable (i.e., 90% identical species that alter specificity), the inoperability of a single embodiment does not warrant a finding that the specification fails to enable the claims under 35 U.S.C. § 112, first paragraph. In fact, the Court of Appeals for the Federal Circuit addressed this very issue of enablement when it stated that "[e]ven if some of the claimed combinations were inoperative, the claims are not necessarily invalid. 'It is not a function of the claims to specifically exclude...possible inoperative substances..." *Atlas Power Co. v. E.I. du Pont de Nemours & Co.*, 750 F.2d 169, 1576 (Fed. Cir. 1984).

In addition, Applicants assertions regarding the state of the art in Section V, above, are herein incorporated and applied.

VIII. Claims 8, 11, 14-22, 24, 26, 27, 30-34, and 37 are Definite under 35 U.S.C. § 112, Second Paragraph

At page 30 of the Office Action, the Office rejects claims 1-3, 6-19, 22, 24, 26, 27, 30-34 and 37 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite.

The rejection is moot as to claims 1-3, 6, 7, 9, 10, 12 and 13. Solely to advance prosecution, Applicants herewith amend the claims without prejudice or disclaimer. Applicants' Amendment overcomes the rejection. Withdrawal of the indefiniteness rejection is therefore kindly requested.

IX. Claims 1, 6, 19, 22, 24 and 26 are Novel over Zia *et al.*

At page 24 of the Office Action, the Office maintains the rejection of claims 1, 6, 19, 22, 24 and 26 under 35 U.S.C. § 102(b) as allegedly being anticipated by Zia *et al.* (*Journal of Cellular Biochemistry Supplement*, 24:269-275 (1996).

The rejection is moot as to claims 1 and 6. Solely to advance prosecution, Applicants herewith amend the claims without prejudice or disclaimer. Applicants' Amendment overcomes the rejection. Withdrawal of the anticipation rejection is therefore kindly requested.

X. Claims 1, 6, 19, 22, 24 and 26 are Novel over Rohlik *et al.*

An page 25 of the Office Action, the Office maintains rejection of claims 1, 6, 19, 22, 24 and 26 under 35 U.S.C. 102(b) as allegedly being anticipated by Rohlik *et al.* (*Biochemical and Biophysical Research Communications*, 149:276-281 (1987)).

The rejection is moot as to claims 1 and 6. Solely to advance prosecution, Applicants herewith amend the claims without prejudice or disclaimer. Applicants' Amendment overcomes the rejection. Withdrawal of the anticipation rejection is therefore kindly requested.

XII. Claims 1-2, 24, 26-27, 30, 32 and 34-36 are Novel over Rohlik *et al.* in view of Teicher *et al.*

At page 26 of the Office Action, the Office maintains rejection of claims 1-2, 24, 26-27, 30, 32 and 34-36 under 35 U.S.C. § 103(a), as allegedly being unpatentable over Rohlik *et al.*

The rejection is moot as to claims 1 and 2. Solely to advance prosecution, Applicants herewith amend the claims without prejudice or disclaimer. Applicants' Amendment overcomes the rejection. Withdrawal of the anticipation rejection is therefore kindly requested.

XII. Claims 1 and 37 are Novel Over Zia *et al.* in view of Queen *et al.*

At page 27 of the Office Action, the Office maintains rejection of claims 1 and 37 under 35 U.S.C. §103(a) as allegedly being unpatentable over Zia *et al.*, in view of Queen *et al.* (U.S. Patent 5,530,101 (issued June 25, 1996)).

The rejection is moot as to claim 1. Solely to advance prosecution, Applicants herewith amend the claims without prejudice or disclaimer. Applicants' Amendment overcomes the rejection. Withdrawal of the obviousness rejection is therefore kindly requested.

XIII. Claims 1 and 37 are Novel Over Rohlik *et al.* in view of Queen *et al.*

At page 28 of the Office Action, the Office maintains rejection of claims 1 and 37 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Rohlik *et al.*, in view of Queen *et al.*

The rejection is moot as to claim 1. Solely to advance prosecution, Applicants herewith amend the claims without prejudice or disclaimer. Applicants' Amendment overcomes the rejection. Withdrawal of the obviousness rejection is therefore kindly requested.

XIV. Claims 1-3, 24, 26-27 and 30-31 are Novel Over Zia *et al.* in view of Lam *et al.*

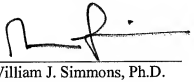
At page 31 of the Office Action, the Office newly rejects claims 1-3, 24, 26-27 and 30-31 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Zia *et al.*, in view of Lam *et al.* (*HKMJ*, 5(2):180-186 (1999)).

The rejection is moot as to claims 1-3. Solely to advance prosecution, Applicants herewith amend the claims without prejudice or disclaimer. Applicants' Amendment overcomes the rejection. Withdrawal of the indefiniteness rejection is therefore kindly requested.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The U.S. Patent and Trademark Office is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



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